



#3

PATENT  
Attorney Docket No. FORS-06443

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Fors *et al.*

Serial No.: 09/929,135

Filed: 08/14/01

Entitled: **Electronic Medical Record, Library of Electronic Medical  
Records Having Polymorphism Data, and Computer Systems  
and Methods for Use Thereof**

Group No.:

Examiner:

**PRELIMINARY AMENDMENT**

Assistant Commissioner for Patents  
Washington, D.C. 20231

**CERTIFICATE OF MAILING UNDER 37 C.F.R. § 1.8(a)(1)(i)(A)**

I hereby certify that this correspondence (along with any referred to as being attached or enclosed) is, on the date shown below, being deposited with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Box Sequence, PO Box 2327, Arlington, VA 22202.

Dated: Feb 19, 2002

By: Marilyn Moy  
Marilyn Moy

Sir or Madam:

This is responsive to the Notice to File Missing Parts mailed on December 18, 2001 setting two months for response which ends on February 18, 2001. Prior to examination of the instant application, please amend the application as follows.

Instructions to amend the specification, and replacement or added paragraphs in clean form pursuant to 37 C.F.R. §1.121(b) is included beginning on page 2 of this communication. A marked-up version of the specification's replacement paragraphs pursuant to 37 C.F.R. §1.121(b) is attached as Appendix I.

**CLEAN VERSION OF REPLACEMENT PARAGRAPHS IN**  
**THE SPECIFICATION PURSUANT TO 37 C.F.R. §1.121(b)**

**IN THE SPECIFICATION**

On page 65, please delete the paragraph beginning on line 23 and ending on page 67, line 8, and replace with the following paragraph:

In some embodiments, the software provides a scoring system to indicate the quality (e.g., the likelihood of performance) of the assay designs. In one embodiment, the scoring system includes a starting score of points (e.g., 100 points) wherein the starting score is indicative of an ideal design, and wherein design features known or suspected to have an adverse affect on assay performance are assigned penalty values. Penalty values may vary depending on assay parameters other than the sequences, including but not limited to the type of assay for which the design is intended (e.g., monoplex, multiplex) and the temperature at which the assay reaction will be performed. The following example provides an illustrative scoring criteria for use with some embodiments of the INVADER assay based on an intelligence defined by experimentation. Examples of design features that may incur score penalties include but are not limited to the following [penalty values are indicated in brackets, first number is for lower temperature assays (e.g., 62-64 °C), second is for higher temperature assays (e.g., 65-66 °C)]:

1. [100:100] 3' end of INVADER oligonucleotide resembles the probe arm:

ARM SEQUENCE:

PENALTY AWARDED IF INVADER

ENDS IN:

Arm 1: CGCGCCGAGG (SEQ ID NO:1)	5'...GAGGX or	5'...GAGGXX
Arm 2: ATGACGTGGCAGAC (SEQ ID NO:2)	5'...CAGACX or	5'...CAGACXX
Arm 3: ACGGACGCGGAG (SEQ ID NO:3)	5'...GGAGX or	5'...GGAGXX
Arm 4: TCCGCGCGTCC (SEQ ID NO:4)	5'...GTCCX or	5'...GTCCXX

2. [70:70] a probe has 5-base stretch (i.e., 5 of the same base in a row) containing the polymorphism;
3. [60:60] a probe has 5-base stretch adjacent to the polymorphism;
4. [50:50] a probe has 5-base stretch one base from the polymorphism;

5. [40:40] a probe has 5-base stretch two bases from the polymorphism;
6. [50:50] probe 5-base stretch is of Gs - additional penalty;
7. [100:100] a probe has 6-base stretch anywhere;
8. [90:90] a two or three base sequence repeats at least four times;
9. [100:100] a degenerate base occurs in a probe;
10. [60:90] probe hybridizing region is short (13 bases or less for designs 65-67°C; 12 bases or less for designs 62-64°C)
11. [40:90] probe hybridizing region is long (29 bases or more for designs 65-67°C, 28 bases or more for designs 62-64°C)
12. [5:5] probe hybridizing region length - per base additional penalty
13. [80:80] Ins/Del design with poor discrimination in first 3 bases after probe arm
14. [100:100] calculated INVADER oligonucleotide Tm within 7.5°C of probe target Tm (designs 65-67°C with INVADER oligonucleotide less than < 70.5°C, designs 62-64°C with INVADER oligonucleotide < 69.5°C)
15. [20:20] calculated probes Tms differ by more than 2.0°C
16. [100:100] a probe has calculated Tm 2°C less than its target Tm
17. [10:10] target of one strand 8 bases longer than that of other strand
18. [30:30] INVADER oligonucleotide has 6-base stretch anywhere - initial penalty
19. [70:70] INVADER oligonucleotide 6-base stretch is of Gs - additional penalty
20. [15:15] probe hybridizing region is 14, 15 or 24-28 bases long (65-67°C) or 13,14 or 26,27 bases long (62-64°C)
21. [15:15] a probe has a 4-base stretch of Gs containing the polymorphism

Please insert the attached Sequence Listing as new pages --118-119--.

#### IN THE CLAIMS

Please renumber the Claims pages from pages "118-127" to --120-129--.

**IN THE ABSTRACT:**

Please renumber the Abstract page from page "128" to --130--.

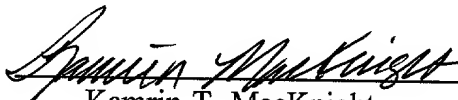
**REMARKS**

The specification has been amended to provide sequence identifiers. Applicants' amendments do not introduce new matter.

The Examiner has requested that a Sequence Listing be provided. Applicants submit this Amendment and Response to provide as a separate part of the disclosure, a "Sequence Listing" pursuant to 37 C.F.R. §§ 1.821-1.825. Applicants submit herewith in paper copy and on floppy disk the Sequence Listing in computer readable form. The contents of the paper and computer readable copies are the same and include no new matter.

Applicants respectfully request entry of this Preliminary Amendment prior to examination of the present application.

Dated: February 19, 2002

  
Kamrin T. MacKnight  
Registration No. 38,230

**Please direct all communication to:**

**Peter G. Carroll**  
**Registration No. 32,837**  
MEDLEN & CARROLL, LLP  
101 Howard Street, Suite 350  
San Francisco, California 94105  
415904.6500

**APPENDIX I**

**MARKED-UP VERSION OF SPECIFICATION'S REPLACEMENT PARAGRAPHS**

The following is a marked-up version of the specification's replacement paragraphs pursuant to 37 C.F.R. §1.121(b) with markings showing changes made herein to the previous version of record of the specification and claims.

**IN THE SPECIFICATION**

On page 65, please delete the paragraph beginning on line 23 and ending on page 67, line 8, and replace with the following paragraph:

In some embodiments, the software provides a scoring system to indicate the quality (e.g., the likelihood of performance) of the assay designs. In one embodiment, the scoring system includes a starting score of points (e.g., 100 points) wherein the starting score is indicative of an ideal design, and wherein design features known or suspected to have an adverse affect on assay performance are assigned penalty values. Penalty values may vary depending on assay parameters other than the sequences, including but not limited to the type of assay for which the design is intended (e.g., monoplex, multiplex) and the temperature at which the assay reaction will be performed. The following example provides an illustrative scoring criteria for use with some embodiments of the INVADER assay based on an intelligence defined by experimentation. Examples of design features that may incur score penalties include but are not limited to the following [penalty values are indicated in brackets, first number is for lower temperature assays (e.g., 62-64 °C), second is for higher temperature assays (e.g., 65-66 °C)]:

1. [100:100] 3' end of INVADER oligonucleotide resembles the probe arm:

ARM SEQUENCE:

PENALTY AWARDED IF INVADER

ENDS IN:

Arm 1: CGCGCCGAGG (SEQ ID NO:1)	5'...GAGGX or	5'...GAGGXX
Arm 2: ATGACGTGGCAGAC (SEQ ID NO:2)	5'...CAGACX or	5'...CAGACXX
Arm 3: ACGGACGCGGAG (SEQ ID NO:3)	5'...GGAGX or	5'...GGAGXX
Arm 4: TCCGCGCGTCC (SEQ ID NO:4)	5'...GTCCX or	5'...GTCCXX

2. [70:70] a probe has 5-base stretch (i.e., 5 of the same base in a row) containing the polymorphism;
3. [60:60] a probe has 5-base stretch adjacent to the polymorphism;
4. [50:50] a probe has 5-base stretch one base from the polymorphism;
5. [40:40] a probe has 5-base stretch two bases from the polymorphism;
6. [50:50] probe 5-base stretch is of Gs - additional penalty;
7. [100:100] a probe has 6-base stretch anywhere;
8. [90:90] a two or three base sequence repeats at least four times;
9. [100:100] a degenerate base occurs in a probe;
10. [60:90] probe hybridizing region is short (13 bases or less for designs 65-67°C; 12 bases or less for designs 62-64°C)
11. [40:90] probe hybridizing region is long (29 bases or more for designs 65-67°C, 28 bases or more for designs 62-64°C)
12. [5:5] probe hybridizing region length - per base additional penalty
13. [80:80] Ins/Del design with poor discrimination in first 3 bases after probe arm
14. [100:100] calculated INVADER oligonucleotide T<sub>m</sub> within 7.5°C of probe target T<sub>m</sub> (designs 65-67°C with INVADER oligonucleotide less than < 70.5°C, designs 62-64°C with INVADER oligonucleotide < 69.5°C)
15. [20:20] calculated probes T<sub>m</sub>s differ by more than 2.0°C
16. [100:100] a probe has calculated T<sub>m</sub> 2°C less than its target T<sub>m</sub>
17. [10:10] target of one strand 8 bases longer than that of other strand
18. [30:30] INVADER oligonucleotide has 6-base stretch anywhere - initial penalty
19. [70:70] INVADER oligonucleotide 6-base stretch is of Gs - additional penalty
20. [15:15] probe hybridizing region is 14, 15 or 24-28 bases long (65-67°C) or 13,14 or 26,27 bases long (62-64°C)
21. [15:15] a probe has a 4-base stretch of Gs containing the polymorphism